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Vanderbilt, AstraZeneca collaborate on new COVID-19 antibody research

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By: Bill Snyder

Vanderbilt University and the global biopharmaceutical company AstraZeneca have signed a new agreement that will enable AstraZeneca to advance two coronavirus-neutralizing antibodies discovered by the Vanderbilt Vaccine Center (VVC) into clinical development as a potential combination therapy for the prevention and treatment of COVID-19.

The agreement announced today builds on the recent collaboration between AstraZeneca, Vanderbilt University and Vanderbilt University Medical Center (VUMC). The VVC is part of VUMC, while ownership of "inventions" by VUMC's employees is assigned to Vanderbilt University (VU) under an intellectual property and associated technology transfer agreement between VU and VUMC.

After evaluating the ability of more than 1,500 monoclonal antibodies to bind and neutralize the COVID-19 virus, SARS-CoV-2, in the laboratory, AstraZeneca signed an exclusive license to six candidate antibodies in Vanderbilt's portfolio. The company plans to progress two of these antibodies into clinical evaluation as a combination approach within the next two months.

The antibodies target two distinct parts of the surface "spike" protein that enables the virus to bind to and fuse with the host cell membrane. The goal is to

neutralize the virus and to limit its ability to infect healthy cells.

“By combining two monoclonal antibodies that bind to distinct parts of the SARS-CoV-2 spike protein into what potentially could be a single preventative therapy, we hope to improve its effectiveness in neutralizing the virus,” said Mene Pangalos, AstraZeneca’s Executive Vice President for BioPharmaceuticals R&D.

“This collaboration helps ensure potential medicines that can prevent or treat COVID-19 are accelerated as quickly and safely as possible,” he said.

“AstraZeneca is a great partner to take some of our lead antibodies into the clinic rapidly and safely because of their deep experience in developing antibodies for human use,” said VVC Director James Crowe, Jr., MD. “Their robust manufacturing and testing capacity are just what is needed in this moment of global crisis.”

Currently there is no effective treatment or vaccine to stop the spread of SARS-CoV-2, which as of today had infected nearly 7 million people worldwide and caused more than 400,000 deaths, 113,000 of them in the United States.

VVC researchers have developed techniques for rapidly isolating clones of white blood cells that make antibodies targeting specific viral proteins. In the laboratory, these “monoclonal” antibodies are then comprehensively examined to identify those rare antibodies with a laser-like focus for finding — and neutralizing — a specific virus.

For the past three months Crowe, Associate VVC Director Robert Carnahan, PhD, and their colleagues have been working around the clock with an international team of academic, governmental and industry partners to identify and analyze antibodies against SARS-CoV-2.

Last month the Vanderbilt researchers reported preliminary findings that potent neutralizing antibodies recognizing unique sites of the spike protein protected mice from consequences of SARS-CoV-2 infection, preventing severe weight loss and reducing viral burden and inflammation in the lung.

The report, which was posted online by the preprint server bioRxiv and which has not yet been peer-reviewed, notes that because the virus can mutate, antibody-based treatments will need to target multiple sites on the spike protein.

"We strongly believe the future of infectious disease treatment will increasingly involve rationally designed therapeutic antibody cocktails like those we have designed with our partners for SARS-CoV-2," Carnahan said. "It has never been more important to both rapidly provide a treatment option and to ensure that it also has future utility as the virus evolves."

In theory, these antibodies could be given as injections to prevent infection, and also to treat and prevent disease progression in people who have already been exposed or infected.

AstraZeneca has stated that the aim of giving two monoclonal antibodies in combination is to increase the efficacy of treatment and reduce the impact of any mutations of the SARS-CoV-2 virus. The Vanderbilt antibodies will be engineered using AstraZeneca proprietary technology to extend their longevity in the body.

Major funding sources for the VVC include the Defense Advanced Research Projects Agency of the U.S. Department of Defense, the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, and the Dolly Parton COVID-19 Research Fund at Vanderbilt.

Crowe holds the Ann Scott Carell Chair in the Departments of Pediatrics and Pathology, Microbiology and Immunology in the Vanderbilt University School of Medicine. Carnahan is an associate professor of Pediatrics.

Other Vanderbilt co-authors were Seth Zost, PhD, Pavlo Gilchuk, PhD, Elad Binshtein, PhD, Joseph Reidy, Andrew Trivette, Rachel Nargi, Rachel Sutton, Naveen Suryadevara, PhD, Taylor Jones, Samuel Day and Luke Myers.